Value of single photon emission computerized imaging in the treatment of patients undergoing carotid endarterectomy

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Purpose: The purpose of this study was to evaluate the clinical relevance of regional cerebral blood flow by single photon emission computerized imaging (SPECT) in patients undergoing carotid endarterectomy (CEA).
Method: Eighty-four patients were included in this study; 74 were undergoing CEA. All 74 operative cases had SPECT scans before and after surgery. The first 30 patients undergoing CEA also had computed tomography scans for comparison. Findings were correlated during surgery with carotid stump pressures.
Results: No deaths and no strokes occurred. Four complications were seen. In the first 30 patients with computed tomography scans, 20 had positive SPECT scans, whereas the computed tomography scan was negative. A 100% linear correlation was seen with operative stump pressures, and decreased regional cerebral blood flow was noted on SPECT scan before surgery (48 abnormal with mean 26 mm). These patients received shunts during CEA.
Conclusion: SPECT scans add useful physiologic data to anatomic images and provide factual or objective information that is valuable in treating patients undergoing CEA. A positive SPECT scan is predictive of poor collateral circulation and may possibly identify those "at risk," if they have no symptoms, and those who will require shunting during surgery. SPECT scans may facilitate case selection in severe bilateral carotid stenosis and deferment of operation in elderly patients at high risk. After surgery SPECT scans will document the value of successful CEA in reestablishing normal regional cerebral blood flow. Finally, SPECT scans have potential value for reevaluating patients who have complete carotid occlusion for external carotid/internal carotid artery bypass. (J Vasc Surg 1996;24:219-25.)

Recent technology provides a method to perform computer-generated tomographic images of the brain. The SPECT scan (single photon emission computerized imaging), when combined with the new radioisotopic lipophilic perfusion agents, can accurately assess regional cerebral blood flow (rCBF) with a practical, safe, relatively inexpensive technique compared with older methods previously available only in the research environment. This addition of physiologic data on rCBF to the anatomic images should provide more factual or objective information for the physician or surgeon treating patients undergoing carotid endarterectomy (CEA). The value of this new approach is assessed in this clinical study.

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METHODS

Our current evaluation of patients for CEA has included the SPECT scan from October 1992 to January 1994. Eighty-four patients have been studied with baseline (resting) SPECT scans and acetazolamide (ACZ-Diamox) enhancement (stress test). Of these 84 patients, 74 have undergone elective surgery, CEA. The studies were conducted within 1 week before surgery and 1 to 2 weeks after surgery.

This was a personal clinical study of 84 patients with advanced atheromatous disease of their carotid arteries evaluated at the Peninsula Medical Center in Burlingame, California. Patient assessment consisted of carotid duplex scan, Doppler spectral velocity

analysis, and in three indicated cases digital subtraction angiography or elective angiography. The percentage of carotid stenosis was based on these data. Both computed tomography (CT) and SPECT scans of the brain were performed in the first 30 cases; only SPECT scans were performed in the subsequent 54 cases. These scans were compared and correlated with the operative findings including stump pressures in those 74 patients undergoing CEA. The degree of carotid stenosis was 70% to 90% in 54 patients (greater than 80% in 34 of these cases). Twenty patients had critical carotid stenosis greater than 90% by preoperative assessment. During the postoperative follow-up period all 74 patients had SPECT scans after CEA. Ten of the 84 patients included in this study did not undergo CEA.

Demographics. Of the 84 patients, 22 were women, and 62 were men; the mean age was 68 years with a range from 58 to 85 years. Clinical indications for CEA in the 74 operative cases were transient ischemic attack (including amaurosis fugax) in 58 patients, recovered stroke in 5, stroke-in-evolution in 1, and asymptomatic, severe, or critical stenosis in 10. The 10 patients who did not undergo surgery in this study were six older patients with serious medical problems who had asymptomatic 70% to 80% internal carotid artery stenosis with negative enhanced SPECT scans and four patients with stroke who were deferred.

SPECT scan definitions. Positive scan was defined as (1) both resting and enhanced scan show a defect (fixed deficit), and (2) resting scan negative, enhanced scan positive (physiologic). Negative scan was defined as resting scan normal, no defect seen on enhanced scan (no fixed or physiologic deficit).

The protocol for SPECT imaging followed that described previously by Burt et al.[1,2] The radionuclide image-perfusion scans used the lipid-soluble radiopharmaceutical hexamethyl propyleneamine oxine (HMPAO). This is marketed commercially as Ceretec (Medi + Physics [Amersham], Arlington Heights, Ill.). The isotope used was technetium Tc99m, which when combined with exametazime (HMPAO) crosses the intact blood-brain barrier and remains fixed in the neurons for approximately 6 hours. There are no known contraindications or risks, and the amount of radiation is equivalent to an enhanced CT scan. A critical park of this technique is acetazolamide (ACZ) (Diamox. Lederle Lab Division, Pearl River, N.Y.) enhancement of cerebral perfusion. ACZ may increase CBF through vasodilation by up to 80% with a peak effect approximately 30 to 45 minutes after injection. The injection of HMPAO at this time reflects, by retention of the tracer, the CBF reserve.[3] In patients with a significant internal carotid artery stenosis there will be decreased delivery of the isotope to the cerebral cortex distal to the stenosis. This will appear as a relative deficit of the tracer (Tc99m) on the tomographic views (Fig. 1). The loss of vascular reserve can be easily demonstrated by SPECT techniques with tomographic sections (0.5 to 1.0 cm) that can be reconstructed by the computer, allowing comparison of the relative perfusion of the right and left hemispheres (symmetry vs asymmetry). All 74 patients undergoing CEA had resting (control) and ACZ (stress) SPECT scans for comparison before and after surgery. The interpretation of the Siemens Rainbow color image display has been well described in a recent publication[4] with its relevance to rCBF (Siemens Medical Systems, Iselen, N.J.). This color coding adds another technical dimension, aiding accuracy in interpretation of SPECT scans.

RESULTS

No operative deaths or strokes occurred in the 74 patients undergoing CEA. One neurologic deficit persisted in the patient who underwent operation for stroke-in-evolution (persistent hand paresis in a patient with acute right hemiparesis before surgery). Four complications occurred: one perioperative myocardial infarction, one case of serious arrhythmias, one transient ischemic attack, and one reversible ischemic neurologic deficit differentiated from a stroke after surgery with the SPECT scan.

The SPECT scans were compared with the CT scans in the first 30 patients undergoing CEA. The enhanced SPECT scan showed abnormal regional perfusion or decreased regional vascular reactivity distal to the carotid stenosis in 20 of these 30 patients before surgery who had normal CT scans. After the operation (CEA) was performed, the SPECT scan became normal in these 20 patients, indicating improved perfusion in the region that formerly had shown decreased vascular reactivity.

After the first 30 patients CT scans were no longer performed; they were replaced by SPECT scans in the preoperative evaluation of the subsequent 54 patients in this clinical study. Of these later 54 cases, 44 underwent CEA. Postoperative SPECT scans again showed improvement in rCBF in 28 patients who had had evidence of decreased cortical perfusion on enhanced SPECT scans before surgery (Fig. 2). As mentioned previously, 10 patients were assessed before surgery but did not undergo operation. The six patients with a stroke history had no change in their scan. The remaining 10 patients in this series under-

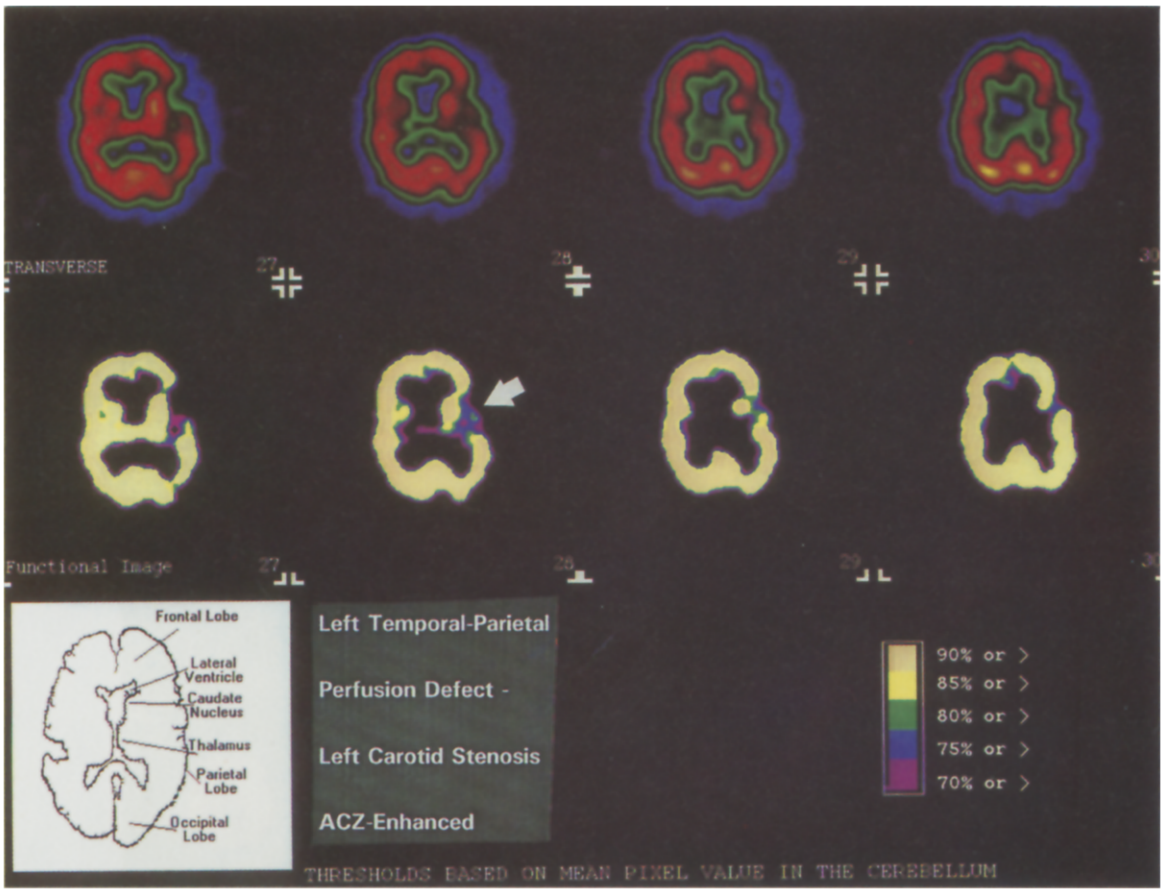

Fig. 1. SPECT SCAN - ACZ enhancement. Preoperative *(L)* cortical perfusion defect (Ischemia).

went CEA with normal scans before and after surgery.

At surgery carotid stump pressures were correlated in all 74 patients and were found to be less than 50 mm mean pressure in the 48 cases who had decreased rCBF shown to some extent in the enhanced SPECT scan before surgery. Therefore these patients had an intraluminal carotid shunt placed during the CEA to provide adequate cerebral blood flow during the endarterectomy. In these 48 patients with abnormal (<50 mm mean) stump pressures, the mean pressure was 26 mm with a range of 9 to 37 mm. In contrast, the other 20 patients who underwent CEA and had normal enhanced SPECT scans before surgery had stump pressures greater than 50 mm and therefore did not receive shunts. Six patients had a stroke history associated with positive resting scans before surgery and therefore received shunts electively. In two of the patients who had recovered from stroke and were undergoing CEA, the SPECT scan differentiated a new from an old infarction in one but added no additional information over the CT scan in the other.

DISCUSSION

The SPECT brain scan with ACZ enhancement is analogous to the persantine-thallium evaluation of the heart. Currently underused, the SPECT scan potentially could add a new, significant, clinical dimension in the evaluation of patients for CEA. Early reports are limited, and the value of the technology is still being defined.[1-11] Pertinent articles in the literature relevant to this subject were recently reviewed in an excellent article by Cikrit et al.[4] as our clinical study was being conducted.

The anatomic condition of a carotid artery stenosis (e.g., percent stenosis on arteriography) does not always correlate with the hemodynamic significance of the lesion.[6] Vasodilation, autoregulatory mechanisms, and collateral circulation all play important roles; therefore physiologic data regarding rCBF

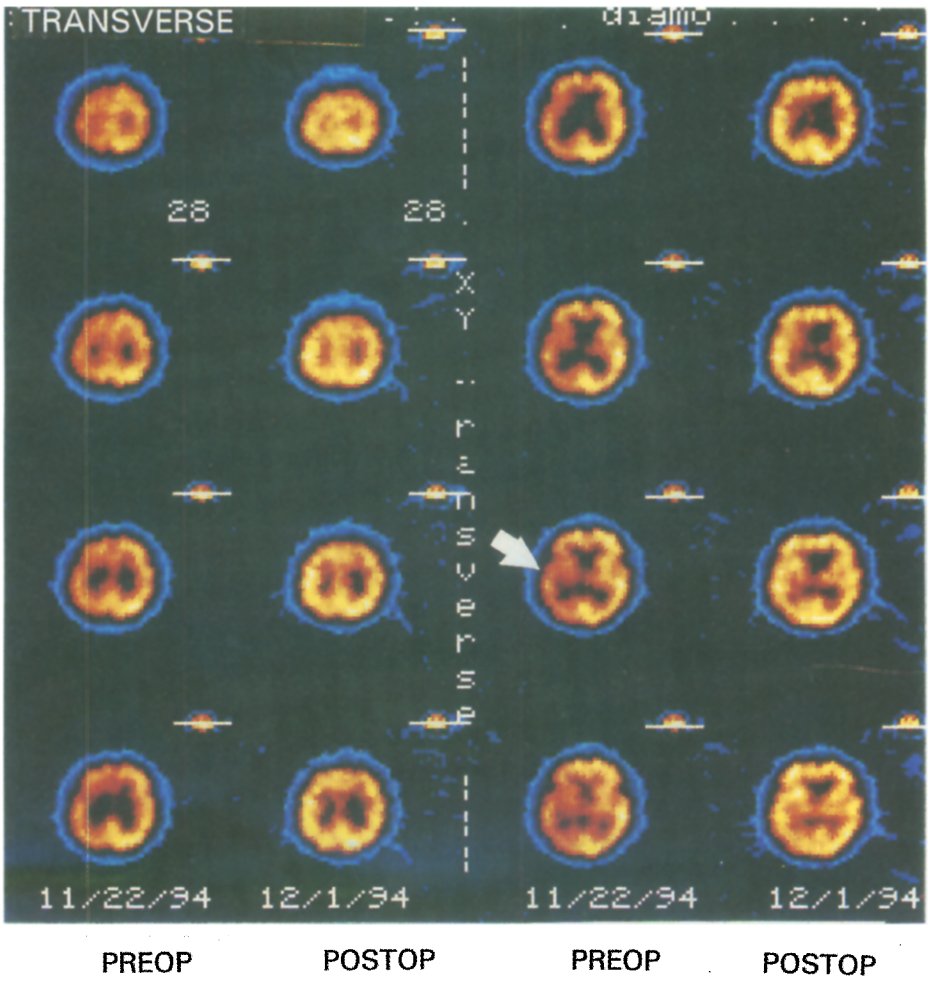

Fig. 2. SPECT SCAN - ACZ enhancement. 80% asymptomatic right carotid stenosis. Postoperative reperfusion of *(R)* cortex.

would be beneficial in case selection for CEA and for assessment of risk and results. For example, the knowledge of ischemic areas may possibly identify patients at high risk. The SPECT scan has the capability of demonstrating ischemic areas not shown by CT scan, and these areas generally correlate with the neurologic symptoms.[7] For example, in the early part of our series 20 of 30 patients undergoing CEA had negative CT scans but positive SPECT scans showing areas of low perfusion (Fig. 1). In addition, at operation all 20 of these patients had low stump pressures (mean 26 mm) and received shunts during CEA. Subsequently 28 other patients had the same linear correlation. In our experience with 48 cases, the predictive value has been 100%. Furthermore SPECT scans in these patients after surgery showed redistribution of rCBF to the identical low perfusion (ischemic) area seen before surgery (Fig. 2). Functional reserve and vascular reactivity were restored to normal in these patients after successful CEA was performed, even to the contralateral cortex distal to a complete carotid occlusion (Fig. 3).

It appears then that the assessment of rCBF is useful in the evaluation of cerebral vascular disease and that SPECT scans with ACZ enhancement can identify areas of decreased vascular flow reserve in patients with normal CT scans.[8] Our study showed a higher correlation than others, perhaps because of the advanced degree of carotid stenosis at the time of referral for CEA. Only 20 of our patients who underwent CEA had stenosis smaller than 80% as judged by duplex scan, spectral velocity analysis, and carotid digital subtraction angiography or selective angiography. Thirty-four had internal carotid artery stenoses greater than 80% and 20 greater than 90%.

In a recent editorial critiquing this emerging

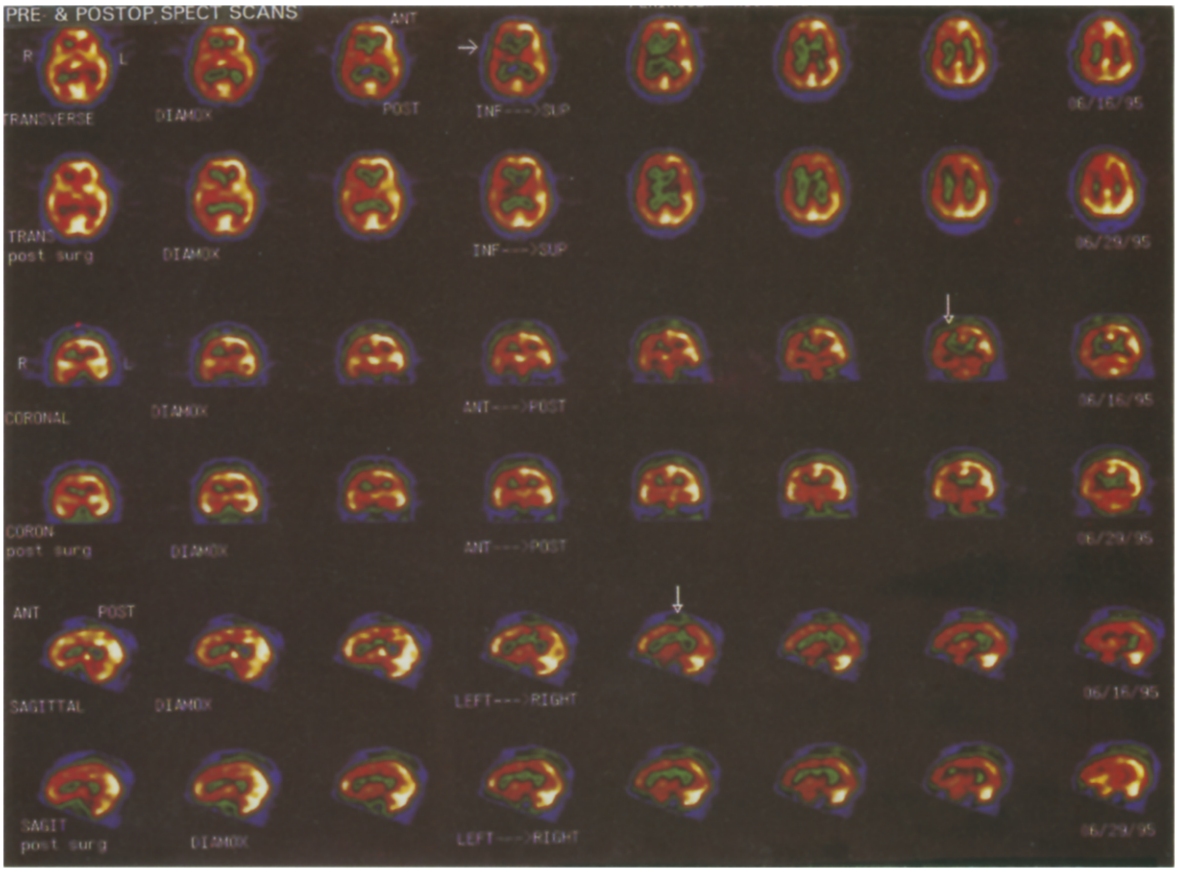

Fig. 3. Reperfusion of contralateral cortex distal to right carotid occlusion after successful left CEA.

technology, Machac and Vallabhajosula[12] emphasize the importance of diagnosing "silent" cerebrovascular insufficiency and offer four prerequisites to assess the efficacy of current SPECT scan technology. First, it requires a suitable radionuclide tracer that will "unmask" intracerebral disease not compensated by collateral circulation during "stress testing." In our study we found that technicium-labeled HMPAO was such a useful agent for reproducing useful anatomic and physiologic data. Subsequently we have used a newer agent, Neurolite (Dupont Pharma, Bellirica, Mass.), which is a more stable radio-pharmaceutical and renders high-definition images.

The second requirement is to induce sufficient vasodilation to detect hemodynamically significant vascular (carotid) lesions. We found ACZ (Diamox) enhancement valuable in this respect, analogous to persantine and thallium in cardiac "stress testing." As a pharmacologic agent for cerebral vasodilation, ACZ was safe, well tolerated, and yielded significant physiologic data to compare with the "resting" baseline SPECT scan. The 100% linear correlation we observed with carotid stump pressures at surgery associated with preoperative areas of low vascular perfusion seen on scans offered a consistent, reliable predictability for shunting during surgery and identified a subgroup potentially "at risk" for stroke when the cerebral vascular insufficiency was "silent" (e.g., asymptomatic carotid stenosis). It is noteworthy that reperfusion of these areas of low rCBF after successful CEA was documented in all ACZ-SPECT scans after surgery.

The third requirement mentioned by the editors for successful cerebral stress testing would be the application of this diagnostic tool to therapeutic or interventional modalities. In our study 74 patients underwent CEA, and 10 had no symptoms. Enhanced SPECT scans aided greatly in identifying those patients "at risk" who had no symptoms and low rCBF. Also, this technique was a valuable screening tool in evaluating those patients with bilateral carotid stenoses who were at high risk but had adequate collateral circulation by stress testing, therefore making the decision not to operate easier, be-

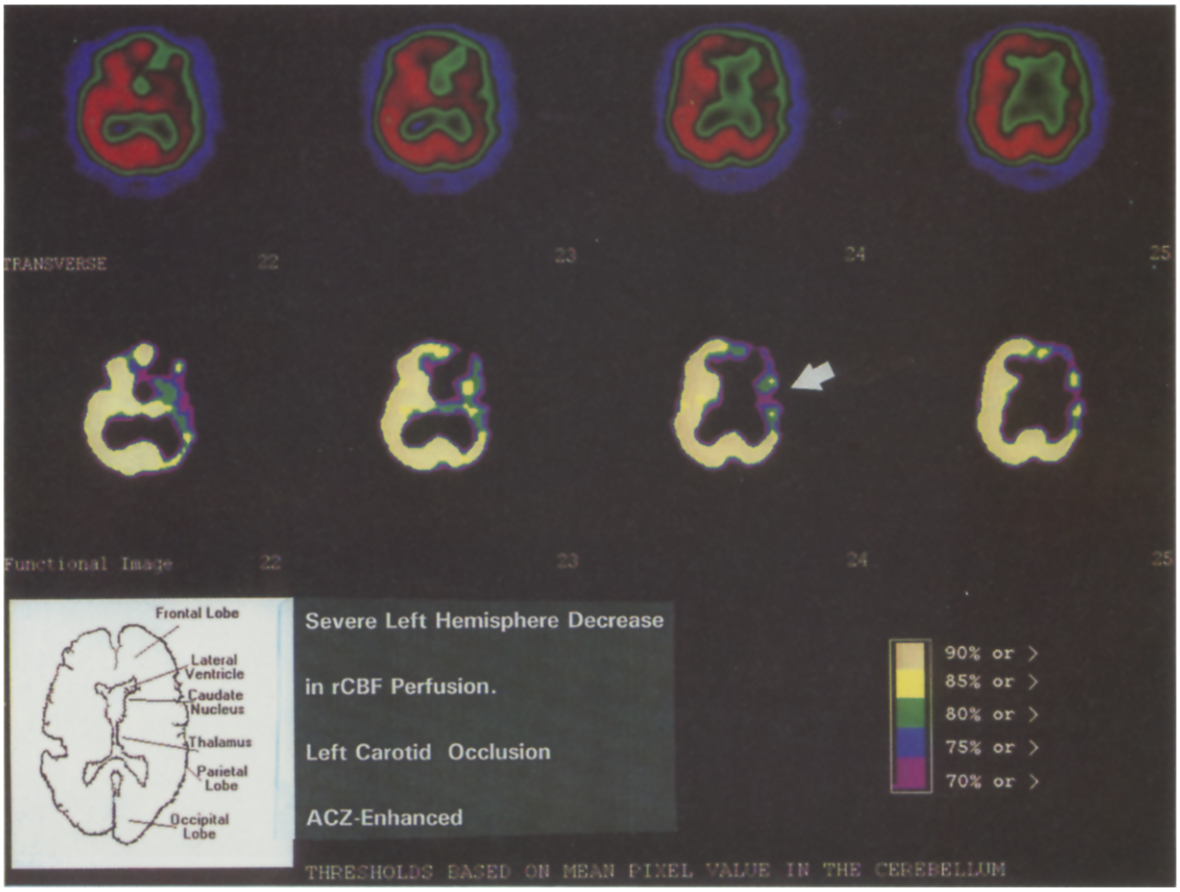

Fig. 4. Massive perfusion defect left cerebral hemisphere distal to occluded carotid (ACZ-enhanced).

cause these patients were not at the same relative risk as those with decreased rCBF distal to their carotid stenosis. Another consideration is future use of enhanced SPECT scans for screening patients with occluded carotid artery(s) to sort out potential candidates for external carotid/internal carotid artery bypass, thus reviving interest in this abandoned procedure that may yet have some clinical relevance (Fig. 4).

The fourth criterion for assessing the value of this relatively new and underused imaging technique is whether it will provide unique and essential information not offered by other technology. As mentioned previously, in our first 30 operative cases 20 had abnormal regional perfusion defects on enhanced SPECT imaging but normal CT scans, which provided the impetus for the change. SPECT imaging adds a physiologic dimension of information not provided by the CT scan. In our hospital a CT scan costs $896 and a SPECT scan $950. The physiological data derived from the SPECT scan favors its choice over the CT scan at this comparable cost in our recent personal experience. Because we do very few carotid arteriographic or digital subtraction angiography studies, this is a cost-efficient workup in conjunction with a Duplex scan.

CONCLUSION

Our study suggests that radionuclide-ACZ-enhanced scanning is helpful in the treatment of patients with cerebral vascular insufficiency. The SPECT scan is valuable because it yields physiologic data of rCBF and provides the same anatomic information as a CT scan. Data derived from enhanced SPECT scans are predictive of poor collateral circulation, correlate well with stump pressures (indicating shunting during CEA), predict those potentially "at risk" with asymptomatic internal carotid artery stenosis (selection criteria), especially bilateral, and documents the value of CEA in reestablishing normal regional cerebral perfusion.

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